

*Decision Neuroscience: Early onset
(childhood) versus adult onset brain
damage, and predisposition to
substance abuse.*

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Objectives:

1. I will provide a brief overview of the brain mechanisms involved in decision-making and impulse control .
2. I will highlight the impact of early versus late onset damage to key neural components subserving decision-making, emotional, and social functioning.

Contrary to the neuroscientific dogma that the earlier the brain damage is, the better the recovery, which is true for some functional systems, like language, the earlier the damage is to systems subserving emotions, the more devastating the consequences in terms of emotional disturbances, risky behaviors, and predisposition to substance abuse.

1. Neural mechanisms of decision-making and impulse control: “willpower”.

Willpower, as defined by the Encarta® World English Dictionary is a combination of determination and self-discipline that enables somebody to do something despite the difficulties involved.

This is the mechanism that enables one to endure sacrifices now in order to obtain benefits later. Otherwise, why should one accept the pain of surgery? Why should one delay gratification or resist temptations?

Loss of “willpower” is the product of an imbalance between two separate, but interacting, neural systems:

(a) An *impulsive, amygdala (and now believe that it is also an insula)-dependent*, system for signaling the emotion of *immediate* prospects

(b) A *reflective, prefrontal cortex-dependent*, system for signaling the emotion of *future* prospects

2) When learning social rules, during development, the reflective system acquires control over the impulsive system via several mechanisms of impulse control.

However, this control is not absolute: there are conditions when (1) the reflective system fatigues (or gets depleted, or (2) bottom-up (body) signals sensitize the impulsive system, so that it overrides the reflective system, and even “hijack” the top-down cognitive resources needed for the normal function of the reflective system, and exercising the willpower to resist stimuli that are tempting (e.g., drugs in the case of addiction).

Control mechanisms of the reflective system:

We distinguish among several separate mechanisms of decision-making and impulse control.

1. Decision-making-May be related to:

Barratt: Non-planning impulsivity (living for the moment-disregard for the future).

Whiteside and Lynam: Premeditation (tendency to think and reflect on the consequences of an act before engaging in that act”.

DECISION-MAKING:

-A dilemma that requires evaluation of pros and cons of various options; there is no clear correct or incorrect answer.

-The process for resolving the conflict engages conscious processing, it is slow, and effortful.

•Example: finding a briefcase with \$100,000 in a dark alley.

You have a very sick aunt that desperately needs an operation and the money saves her life.

Would you keep the money or return it?

Control of emotions (or emotion regulation) may belong to this mechanism.

How do we measure decision-making?

- The IGT.

- There are other paradigms:

 - Cambridge Gambler/ Risk Tasks

 - Game of Dice

 - BART

Neural Substrates?
Decision Making= OFC/VMPC
(especially anterior sector)

Motor
Impulse Control

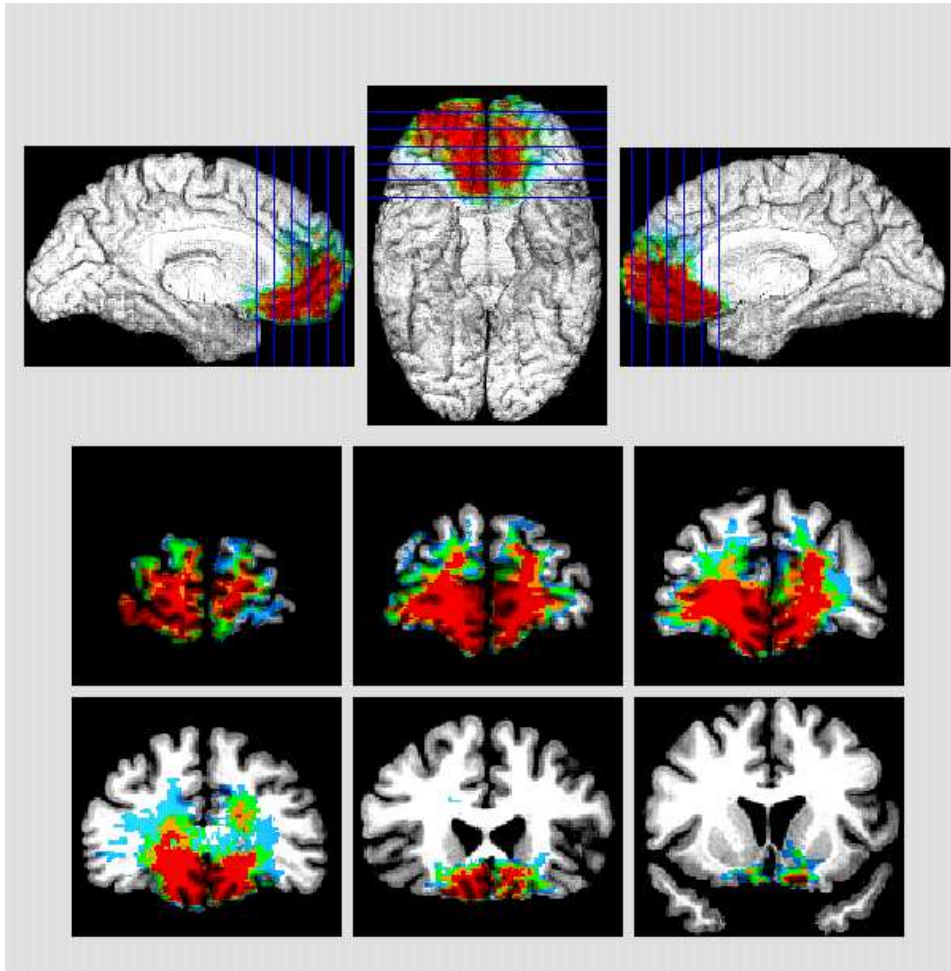
Decision-Making

Ventral Striatum
(nucleus Accumbens)

VTA

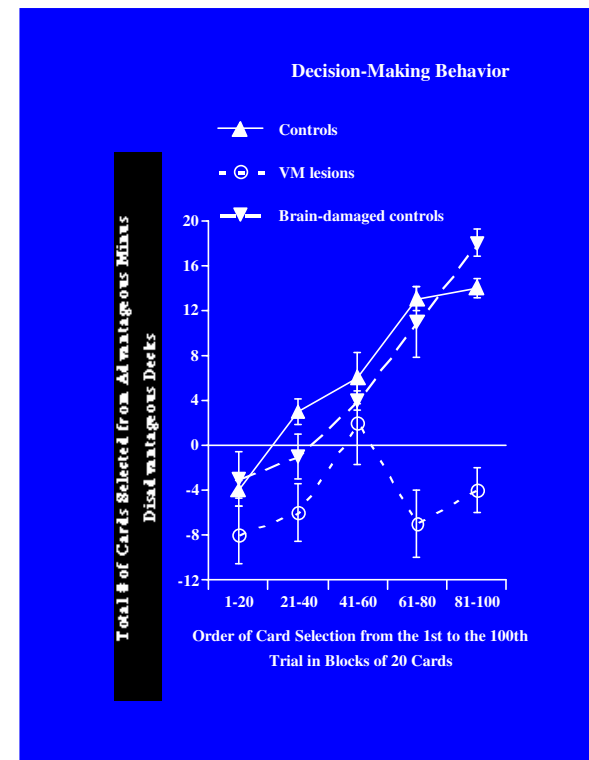
Amygdala

Patients with Orbitofrontal/ VMPC damage:



1. Exhibit many manifestations, including alterations of emotional experience, social functioning, real-life Judgment and decision-making.

2. Perform poorly on the IGT.



2. Motor impulse control (or pre-potent response inhibition):

It concerns the ability to deliberately suppress dominant, automatic, or pre-potent responses.

May be related to:

Barratt: Motor impulsivity (acting without thinking).

Whiteside and Lynam: Urgency (the tendency to experience strong impulses, frequently under conditions of negative affect).

MOTOR IMPULSE CONTROL

This is a mechanism of conflict control or conflict monitoring: At the behavioral/motor response level.

- A learned inhibition that does not require so much evaluation of pros and cons of various response options; there is a clear correct or incorrect answer.
- The process for resolving the conflict is fast, automatic, and relatively effortless.
- Example: finding a pile of \$100,000 spread out on a table inside a bank.

Neural Substrates?
Motor Imp Cont= ACC

Motor
Impulse Control

Decision-Making

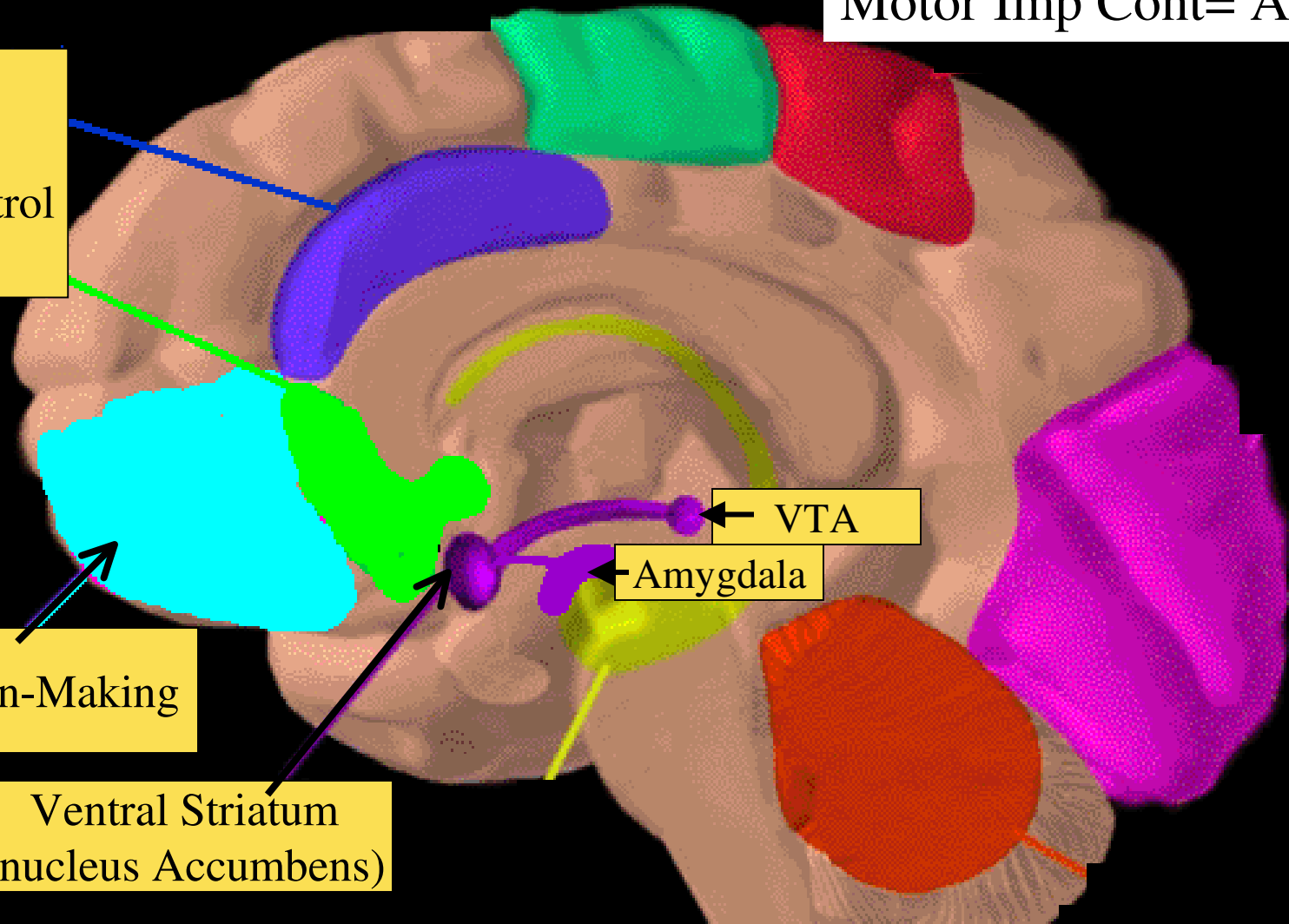
Ventral Striatum
(nucleus Accumbens)

VTA

Amygdala

Measures?

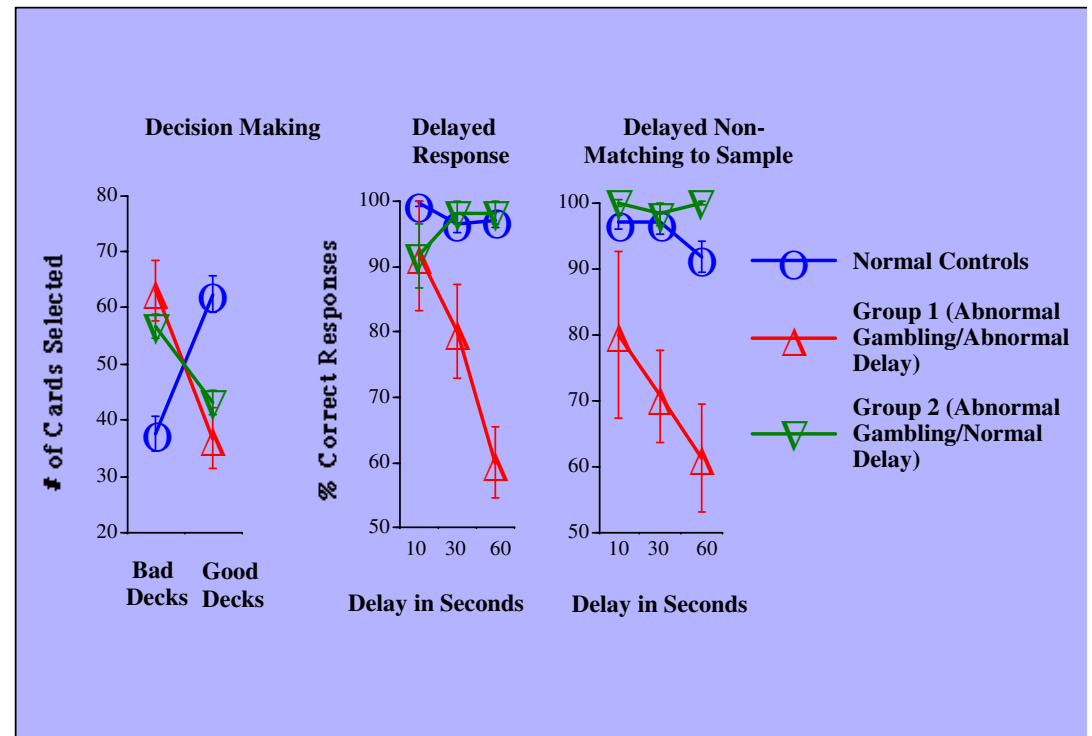
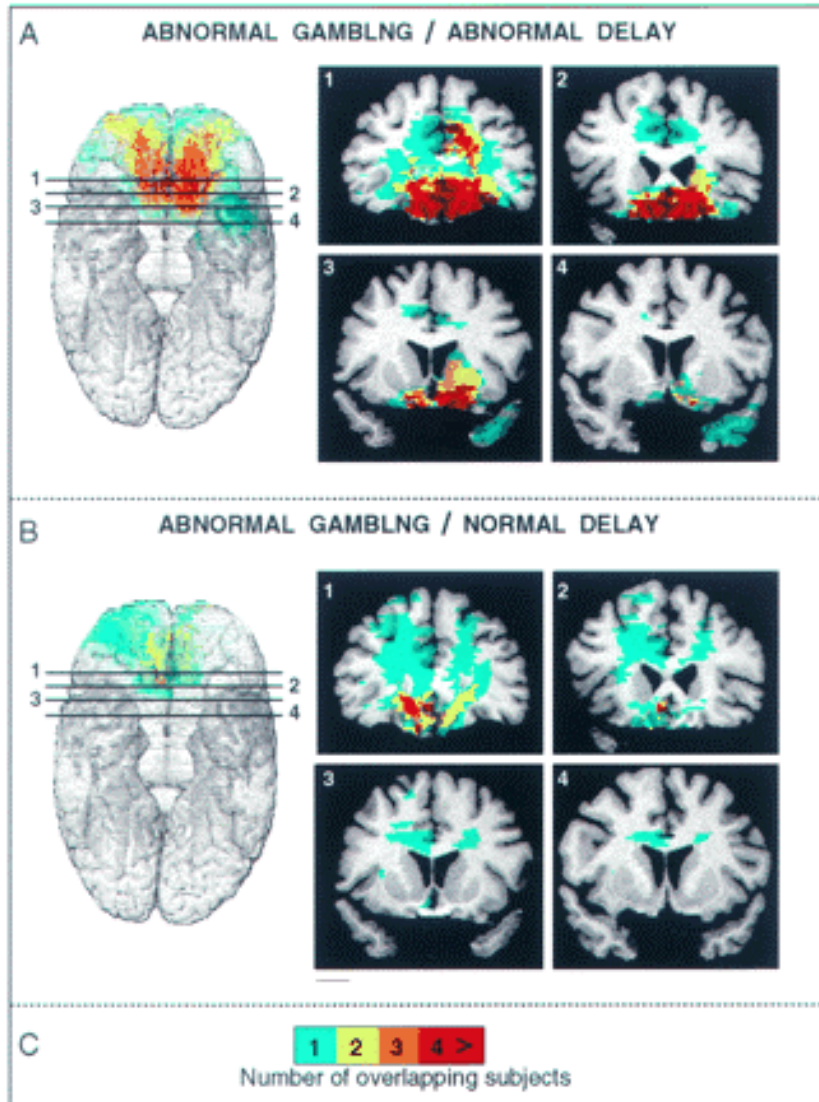
Motor Imp Cont= Go/no Go; Stroop; CPT
Delayed-non-matching to Sample?



More extensive OFC/VMPC damage that involves parts of the ACC:

1. Exhibit additional problems in impulse control, “disinhibition”, and antisocial behavior, e.g., obscene words, grabbing objects not belonging to them.

2. Poor IGT, but in addition, poor DR and DNMS (we think because of poor response inhibition).



3. Cognitive impulse control:

It concerns the ability to inhibit irrelevant thoughts or memories, before or without translation into behavioral (motor) acts.

Difficulties inhibiting particular thoughts, shifting from one thought to another or focusing on one particular thought reflect instances of weakness in this mechanism.

May be related to:

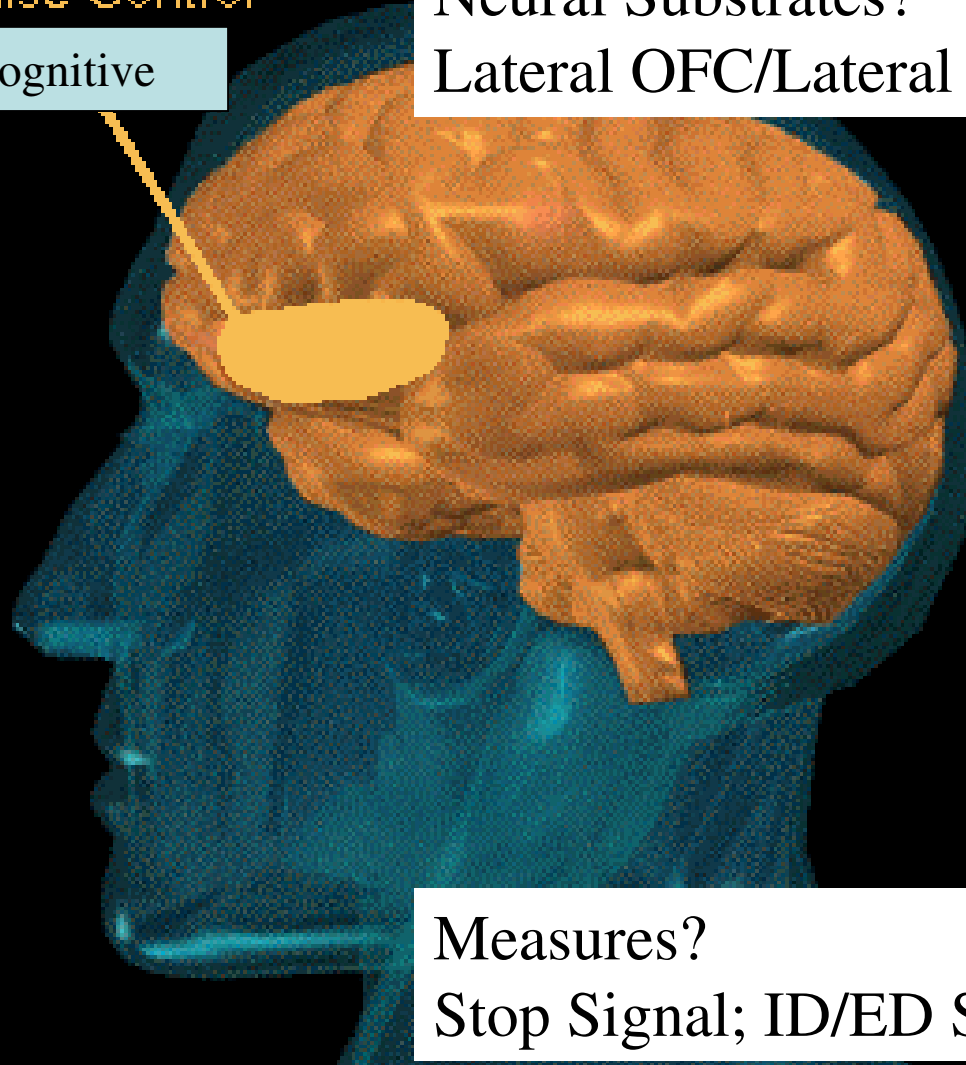
Barratt: Cognitive impulsivity (make up mind quickly; problems concentrating).

Whiteside and Lynam: Perseverance (the ability to remain focused on a task that may be boring or difficult).

Impulse Control

Cognitive

Neural Substrates?
Lateral OFC/Lateral PFC



Measures?
Stop Signal; ID/ED Shift

Overlapping lesions of patients with poor scores on the Stop Signal task revealed:

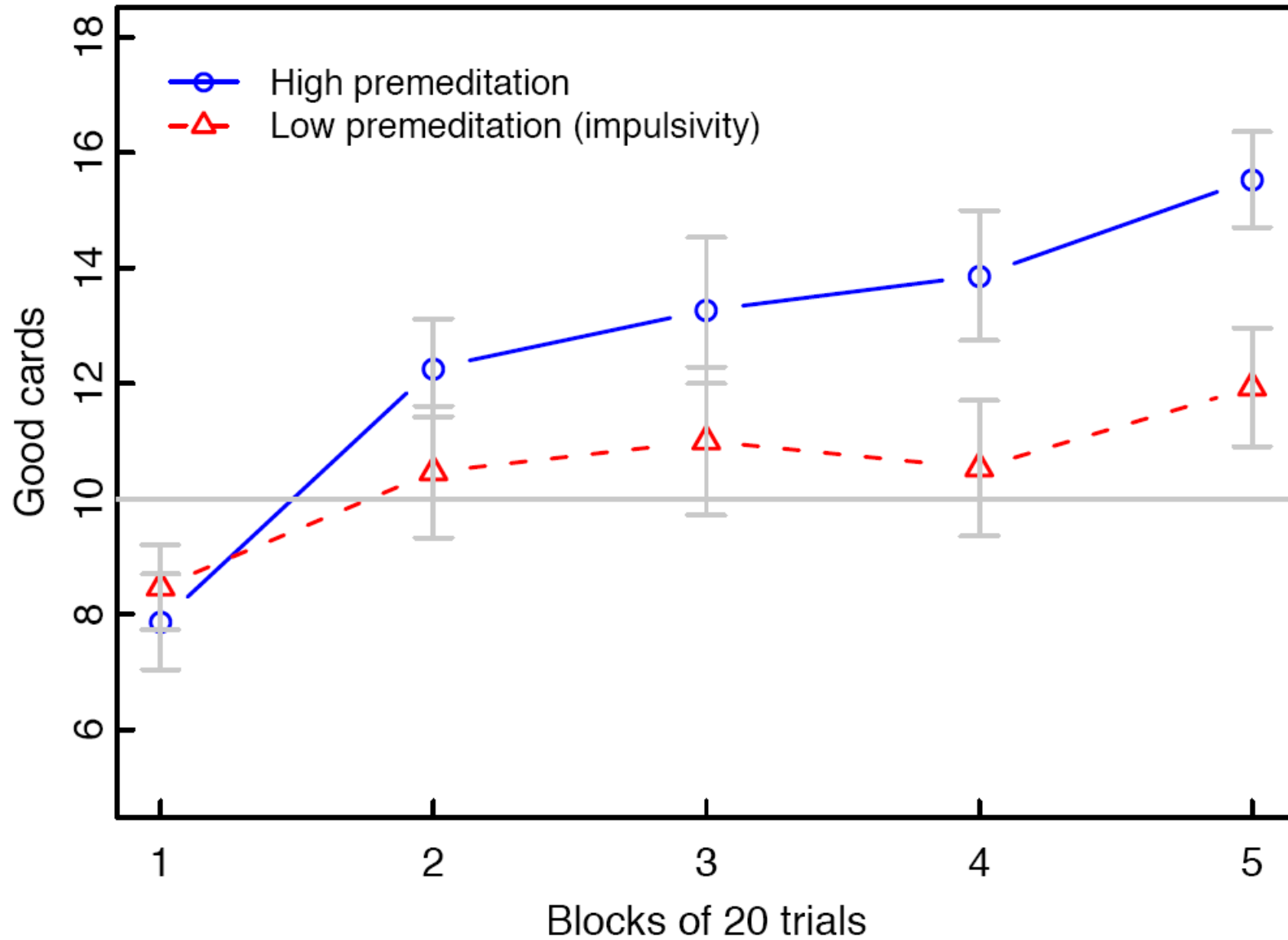
1. Higher degree of overlap in the lateral OFC/inferior frontal gyrus region.
2. But also another region that appeared critical: the insula and surrounding temporal and somatosensory cortices.
Significance? Importance of emotional processing, even in “cold” inhibitions, such as in the Stop Signal Task.

It is very important to realize that although these different control mechanisms can be dissociated under experimental conditions, they are all interrelated and act together in a functioning brain, and difficult to dissociate in normal individuals.

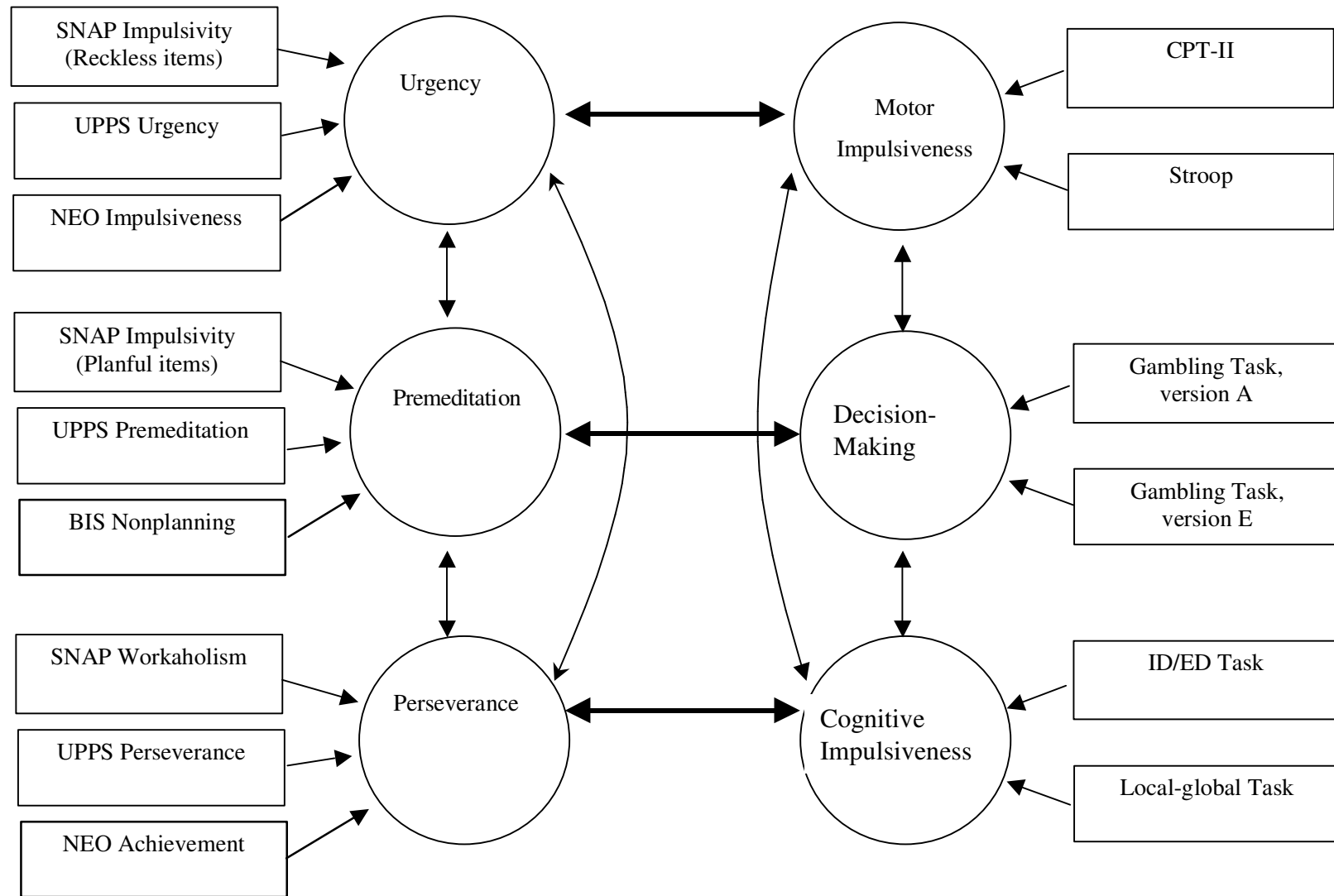
For example, when inhibiting a pre-potent response, such as in the Stroop, it is difficult to do this without engaging mechanisms of cognitive impulse control.

On the relationships between neuropsychological and personality measures of impulsivity. Very little research!

Gambling Task



A more sophisticated approach:



What about Sensation Seeking?

2. Developmental versus Adult Onset Damage:

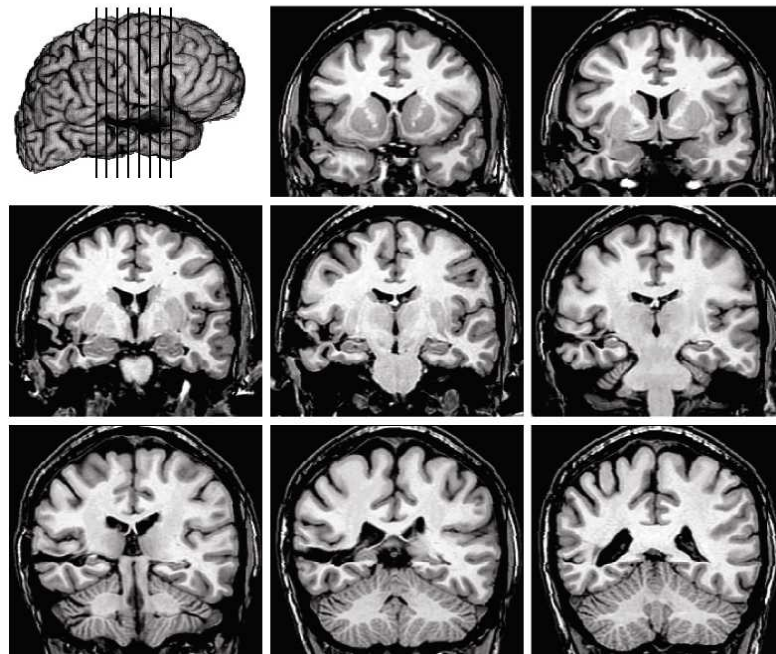
Early onset damage cause more severe behavioral and emotional disturbances than adult onset damage.

No plasticity! No recovery of function!

Although adult-onset damage to these neural systems (e.g., amygdala or OFC/VMPC) can be associated with several behavioral, cognitive, and personality manifestations (e.g., depression, anxiety, impulsivity, and mood disorders) that may predispose individuals to substance abuse, early damage is associated with much more severe disturbances that are co-morbid with substance abuse, including depression, anxiety, impulsivity, as well as severe real-life problems in social conduct, including alcohol and drug abuse.

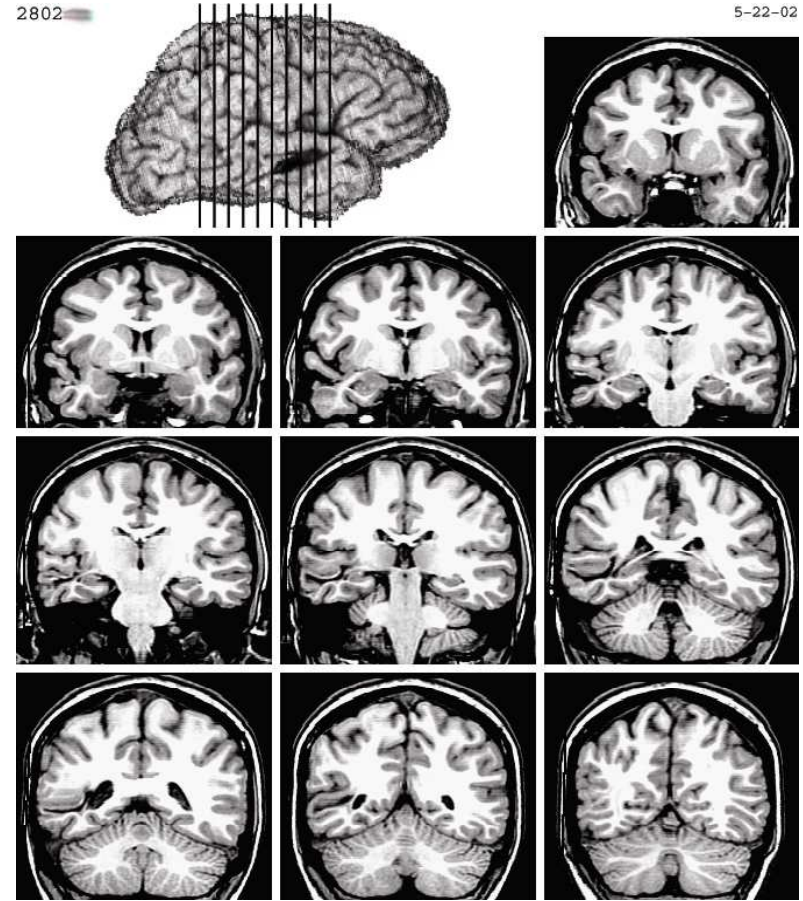
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	Subject 1	Subject 2
<u>Lesion:</u>		
Onset-early age	3 yrs	7yrs
Circumscribed Right temporal uncinate cut	+ Partial	+ complete
Age at time of testing	22 yrs	36 yrs
<u>Cognition</u>	Normal	Normal
<u>Emotion:</u>		
Chronic anxiety	++	+++
Labile	++	+++
Depression	++	++
<u>Behavior:</u>		
Real-life (Antisocial)	++	+++
Substance Abuse	++	+++
impulsivity	++	+++

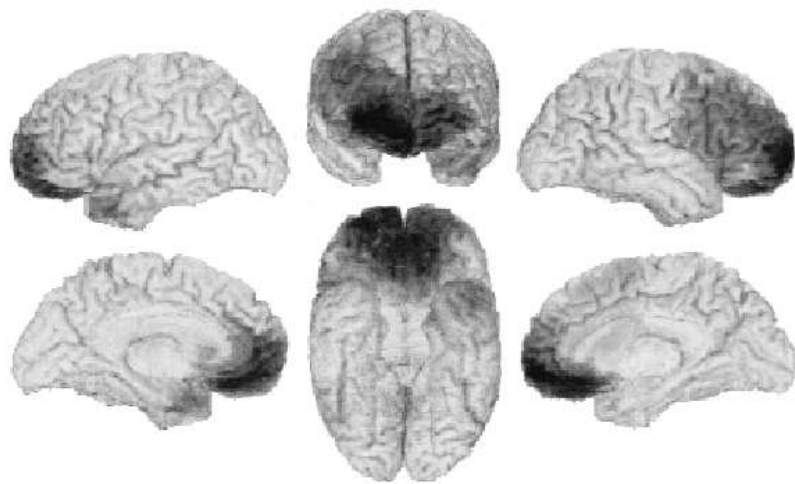
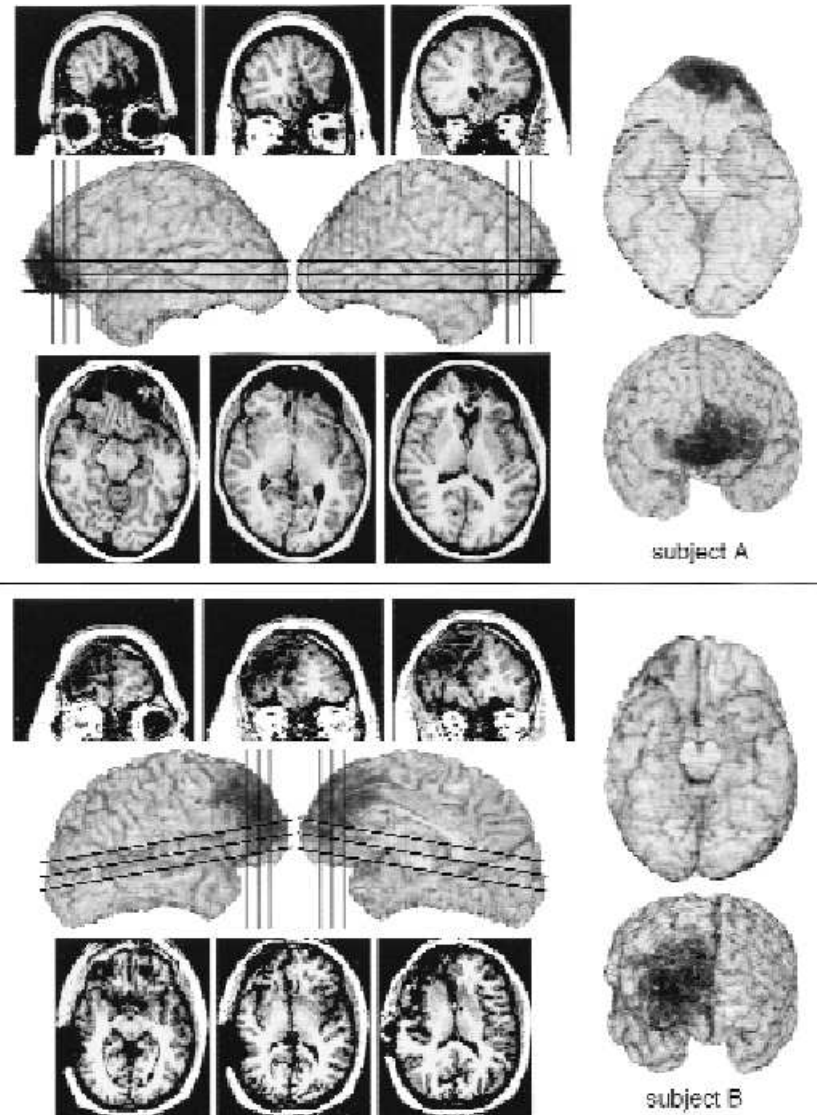


Fig. 4. Control subjects with adult-onset prefrontal damage. The overlap of lesions in the 6 patients with adult-onset lesions is depicted on a normal reference brain. Lesions of individual subjects were transferred onto the reference brain using MAP-3 (ref. 24). Darker shade indicates a higher number of overlapping subjects. The areas involved include all sectors damaged in the target subjects.



	Subject 1	Subject 2
<u>Lesion:</u>		
Onset-early age	15 months	3 months
Age at time of testing	20 yrs	23 yrs
<u>Cognition</u>		
	Normal	Normal
<u>Emotion:</u>		
Chronic anxiety	++	++
Labile	+++	+++
Depression	++	++
<u>Behavior:</u>		
Real-life (Antisocial)	+++	+++
Substance Abuse	+++	+++
impulsivity	+++	+++

The impact of early and late damage to the human amygdala on ‘theory of mind’ reasoning

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Fig. 2 Relationship between the age of damage to the amygdala and overall score on the ToM battery (scores expressed as standard deviations from mean score of healthy comparison group).
Filled black squares = early amygdala damage group (DNETs); filled grey diamonds = late amygdala damage group (surgical excision).

Conclusion:

Relative to adult onset brain damage, focal, and even slight, but early-onset insult to key neural components subserving decision-making, emotional, and social functioning are associated with severe real-life problems in social conduct, especially alcohol and drug abuse, as well as many manifestations co-morbid with substance abuse, including depression, anxiety, impulsivity, and mood disorders.

It is remarkable how the poor recovery from dysfunction of neural systems linked to decision-making, impulse control, and emotional processing goes against the dogma of brain plasticity and recovery of function, which is so robust in many cognitive domains, especially language.

Therefore early detection of disturbances in these neural structures is key.

Early intervention, be it behavioral, pharmacological, or both will avert much more severe problems down the road.